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Percutaneous Catheter Thrombus Aspiration for Acute or Subacute Arterial Occlusion of the Legs: How Much Thrombolysis is Needed?

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Objective: *to evaluate the role of a combined percutaneous endovascular approach including thrombus aspiration, catheter thrombolysis, and percutaneous transluminal angioplasty (PTA) to treat acute and subacute occlusions of native leg arteries.*
Materials and methods: *retrospective evaluation of the effectiveness and safety of this catheter therapy in 89 consecutive patients (93 legs) in a single centre.*
Results: *treatment was initially successful in 90% of legs. Mortality at 30 days was 8%, and at 12 months 19%. Amputation-free survival at 12 months was 78%. Aspiration alone was sufficient in 31% of cases, urokinase (mean dose 112 500 ± 55 900 IU) was used in 22%, PTA was added in 69%. There was no major bleeding except for one false aneurysm treated by ultrasound-guided compression. Secondary interventions within 12 months were required in 30% of cases (14 endovascular, 16 open surgical procedures).*
Conclusions: *catheter thrombus aspiration in combination with thrombolysis and/or PTA is highly effective. Only in a minority of patients are thrombolytics in modest doses necessary, and serious bleeding complications are rare. We recommend this procedure as first-line treatment for acute or subacute infrainguinal arterial occlusions.*

Key Words: Percutaneous catheter thrombus aspiration; Thrombolysis; PTA; Endovascular technique; Amputation-free survival.

Introduction

Percutaneous, catheter-directed thrombolysis has been applied for many years to treat acute arterial occlusions of the legs.[1–8] However, the safety and efficacy of the procedure has continued to give cause for concern. For example, in the TOPAS trial,[9] serious bleeding problems were associated with local thrombolysis, although the patency rates did not exceed those achieved by surgery[5]. Furthermore, in the studies reported hitherto, blood flow is restored more slowly than by immediate surgical revascularisation, and tissue ischaemia may progress to necrosis before thrombolysis has become effective. Therefore, the requirements for an ideal catheter-directed method must envisage the avoidance of haemorrhage together with a substantial reduction of the time necessary for restoring arterial flow comparable to the duration of a surgical procedure.

It is the aim of the present study to demonstrate that, by performing a combined percutaneous endovascular therapy including catheter aspiration, thrombolysis, and percutaneous angioplasty (PTA), high rates of primary success and limb preservation can be achieved. If thrombus aspiration works, thrombolysis may be avoided altogether or reduced. Because we apply thrombolysis, when necessary, by thrombus infiltration, the doses of urokinase may be minimised, and the duration of the intervention shortened. Underlying stenoses detected in the course of the intervention may be treated by balloon angioplasty (PTA) in the same session. The fact that there are only very few publications on percutaneous catheter thrombus aspiration,[10–12] and even less on this combined approach,[10] may explain why the impact of this procedure has so far not been widely recognised.

Methods and Patients

Patient selection

There were 89 consecutive patients (42 men and 47 women), ages ranging from 29 years to 100 years

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Table 1. General baseline characteristics of patients.

Demographics	
Age (years ± SD)	70.7 (±14.9)
Number of patients	89
Gender	
Male	42
Women	47
Risk factors	
History of smoking	39 (44%)
Diabetes	14 (16%)
Hypertension	49 (56%)
Hypercholesterolaemia	17 (19%)
Co-morbidity	
Cardiopathy	45 (50.5%)
Coronary heart disease	41 (46.5%)
Atrial fibrillation	19 (21.5%)
Transient cerebral ischaemia or stroke	14 (16%)
Chronic obstructive pulmonary disease	11 (12.5%)
Pulmonary embolism	9 (10%)
Multifocal arterial embolism	7 (8%)
Renal insufficiency	9 (10%)
Total number of patients with co-morbidity	68 (76%)

Table 2. Vascular baseline characteristics of patients.

Clinical presentation	
Duration of symptoms (days)	6.2 (±7.3)
Pain at rest	89 (100%)
Motor loss	7 (7.7%)
Sensory loss	73 (81%)
Embolism likely	53 (61.7%)
Acute on chronic occlusive disease	40 (49%)
Site of arterial occlusion	
Aa. fem. sup. et poplitea	24
Aa. fem. sup., poplitea et crurales	32
Aa. crurales	26
Aa. profunda fem., fem. sup. et poplitea	9
A. profunda femoris	2
A. fem. sup.	1

(mean age 70.7 ± 14.9 years, 93 legs) with acute or subacute thromboembolic occlusion of native femoropopliteal and crural arteries in 93 legs. They constituted 9% of the patients undergoing catheter therapy in infrainguinal arteries at our institution between January 1995 and May 1997. The indication for catheter therapy was critical ischaemia in all (69 patients presenting with rest pain, and a further 20 patients with trophic lesions as well). Treatment decisions were reached through joint discussions between the vascular surgeons, the interventional radiologists and angiologists.

In this study only patients with occlusions of the infrainguinal native arteries were included.

Catheter therapy was performed urgently (the same day or within 24 h of onset of symptoms) in 33 cases (37.5%), whilst in 45 patients (51%) the acute onset of arterial occlusion was less than 14 days. In the remaining 11 patients (12.5%) the acute episode of occlusive disease was more than 14 days old (range 14–28 days). For the whole group the mean duration between onset of the acute occlusive episode and catheter therapy was 6.2 days (±7.3). A sensory deficit was present in 73 patients, and a motor deficit in seven cases. Twenty legs in patients either with a longer history than 14 days or with subacute or acute-on-chronic disease presented with trophic lesions (21.5%). Baseline patient characteristics and clinical presentation are shown in Tables 1 and 2.

Procedures

Percutaneous thrombus aspiration was performed as the primary procedure in all patients and as single therapy in 29 legs (31%), all of which had embolic occlusion (Fig. 1). In 44 legs (47%) thrombus aspiration was followed by balloon angioplasty (PTA) of underlying atherosclerotic lesions without thrombolysis, and in only 20 legs (22%) was it necessary to use thrombolysis together with aspiration and PTA (Fig. 2).

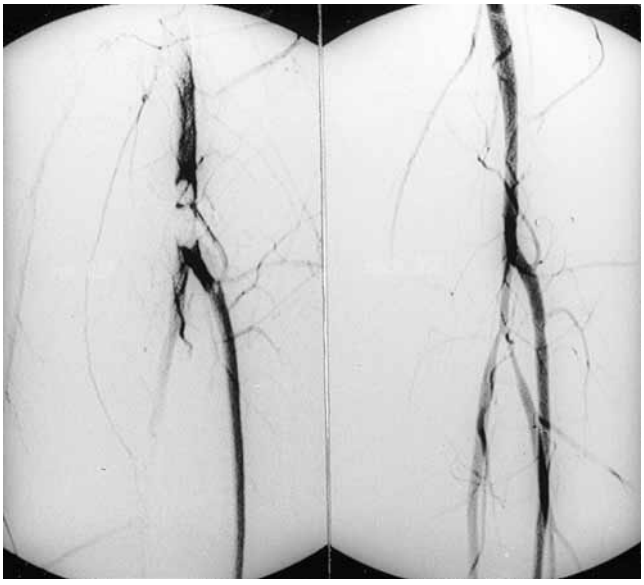

Fig. 1. Acute embolic occlusion of the popliteal and crural arteries before (left panel) and after catheter thrombus aspiration (right panel) as the only interventional method applied.

Intravenous heparin was given for at least 24 h. Thereafter oral anticoagulation was prescribed for 6 months in patients with embolism and in those with local thrombosis. This was followed by platelet inhibitors.

Catheter techniques

Under local anaesthesia, after anterograde puncture catheterisation of the common femoral artery, a 6- or

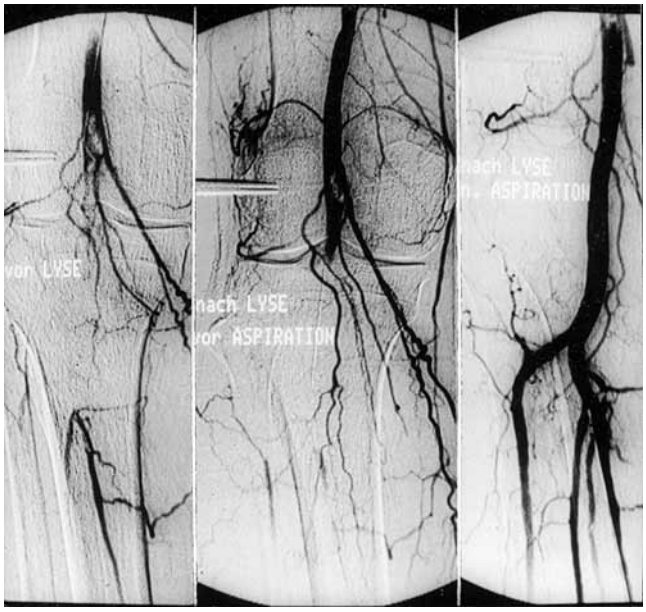

Fig. 2. Demonstration of the combination of thrombolytic therapy with catheter thrombus aspiration. Left panel: Acute occlusion of the popliteal trifurcation with motor and sensory deficit, one day old. Middle panel: After 20 min of intraclot thrombolysis with urokinase (60 000 IU) there was only minor improvement but thrombus aspiration was possible. Right panel: By percutaneous catheter thrombus aspiration complete restoration of patency was achieved within 15 min.

8F introducer sheath with a removable haemostatic valve was introduced.[10,11] A bolus of 5000 IU of heparin was given. In the presence of fresh thromboembolic material a thin-walled 6–8F aspiration catheter with an end-hole was positioned into the proximal end of the thrombus, whereupon the aspiration was performed with a 60-ml syringe. For the extraction of larger pieces of clot, the haemostatic valve had to be removed. By repeating clot extraction all the non-adherent material could be removed, whilst residual thrombotic material adhering to the vessel wall was loosened with an angioplasty balloon or with a wire loop[11,12] and subsequently also sucked out. In the crural arteries 5F aspiration catheters were used. If it was impossible to remove the occluding clot completely, then local catheter thrombolyis was performed in the same session. A 0.035-inch guidewire served to introduce a microporous balloon catheter (Schneider R) down into the proximal part of the thrombus, taking care not to pass beyond the clot in order to avoid peripheral embolism. Through the balloon catheter, urokinase was infiltrated into the thrombus (dosage 10 000–20 000 units per cm of occlusion length). Under fluoroscopic control, the balloon catheter was forwarded centimetre by centimetre until the distal end of the thrombus was reached. Clot material loosened by partial lysis was removed by repeated aspiration. Control angiography was performed to confirm free peripheral outflow; underlying stenotic lesions were thereafter treated by PTA in the same session. Completion angiography was performed before removal of all instruments. Duration of the intervention and total dose of the lytic agents were recorded.

Outcome criteria

Endpoints of the present study were mortality, amputation at 30 days, 6 and 12 months and the amputation-free survival of the entire patient group at 6 and 12 months. Other endpoints were the primary dissolution of occluding thrombus, i.e. primary success and patency rate achieved by the afore-mentioned catheter techniques, and the number and percentage of secondary reinterventions necessary, whether open surgical or by catheter technique. Surgical reinterventions consisted of femorodistal bypasses or thromboendarterectomy, catheter reinterventions included repeated thrombus aspiration with and without adjuvant lytic therapy and PTA, with placement of a stent in one single instance.

With regard to the occurrence of adverse effects of lytic therapy, special attention was given to bleeding complications, including cerebral haemorrhage with or without associated mortality. The individual doses of urokinase used were recorded and related to possible complications. False aneurysms were also sought.

The observation time was 12 months. Two patients with successful catheter treatment were returned to their referring hospital on the same day, whereupon they were lost to follow-up (three legs). The follow-up of 12 months in this study is therefore based on 87 patients and 90 legs, respectively.

Statistical analysis

Quantitative data were expressed as mean values $\pm$ one standard deviation.

Times to events were analysed with Kaplan–Meier analysis (Stata, Release 5, Stata Corporation, College station Texas, 1997). Group differences were assessed with the unpaired Student's *t*-test, and with Mann–Whitney *U*-test for non-parametric groups. A *p*-value less than 0.05 was considered significant.

Results and Clinical Outcome

A summary of the results including primary success, secondary procedures, amputations, and mortality is

Table 3. Results of catheter interventions.

	n	%
Procedures:	93	100
Aspiration only	29	31
Thrombolysis	20	22
PTA	64	69
Primary success	84	90
Secondary procedures	28	30
Endovascular	14	
Surgical	16	
Amputations (6 m)	8	9
Below-knee	5	
Through-knee	1	
Above-knee	2	
Mortality		
30 days		8
6 months		16
12 months		19

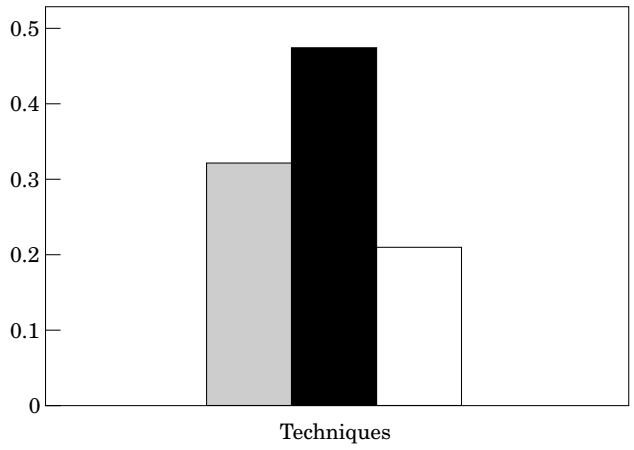

Fig. 3. Percutaneous catheter thrombus aspiration was performed in all patients in this series of 93 legs. It was the single therapy in 31%, and was combined with adjunctive PTA in 47%. In 22% only (white bar) it was necessary to add modest doses of urokinase that gave rise to clot disintegration and facilitated clot aspiration. (▤) Aspiration alone; (■) aspiration + PTA; (□) aspiration + PTA + lysis.

given in Table 3. Application of catheter aspiration alone without additional lysis or PTA, of adjunct thrombolytic therapy, and PTA is illustrated in Fig. 3. The individual doses of urokinase varied between 50 000 and 250 000 IU (mean 112 500 ± 55 900 IU). There were no major bleeding episodes, with the exception of one false aneurysm at a puncture site which was treated successfully by ultrasound-guided compression. No blood transfusions were necessary, and there was no intracranial haemorrhage. Duration of the intervention ranged between 35 and 160 min.

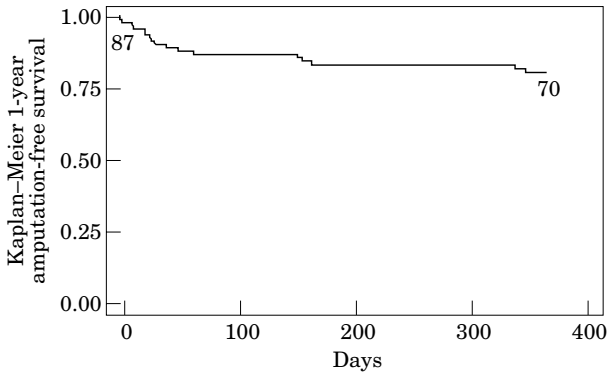

Fig. 4. Kaplan–Meier curve showing 12 month amputation-free survival of the whole patient group.

The amputation-free survival at 6 and 12 months is illustrated in Figure 4.

Whilst for the entire group of 89 patients the acute thrombotic or embolic occlusion of the leg had occurred within 6.2 ± 7.3 days, the arterial occlusion event in 19 patients (20 legs) requiring adjunctive thrombolysis was older (11.15 ± 9.8 days; $p<0.01$). In the 70 patients who did not need thrombolysis (70 patients) the duration of symptoms before treatment was even shorter (4.7 ± 5.6 days; Mann–Whitney *U*-test: $p = 0.0045$).

Discussion

The analysis of the efficacy and safety of percutaneous catheter thrombus aspiration in combination with adjunct thrombolysis and/or PTA of 93 legs in 89 patients shows an initial treatment success in 90% of the legs, a reintervention rate of 30%, an amputation-free survival in 78%, and a mortality rate of 19% at 12 months' follow-up. These results were accomplished by aspiration alone in 31%, by additional thrombolysis in 22%, and by PTA in 69% of the treated legs.

The TOPAS trial, a randomised prospective study comparing local thrombolysis to open surgery reported by Ouriel and associates,[9] demonstrated that thrombolysis reduced the need for secondary open-surgery procedures. Whereas in the TOPAS study 25% of all occlusions were located above the inguinal ligament, and thrombolysis was used for bypass grafts in 55%, the occlusions in our study were all limited to infrainguinal native arteries. The majority of occlusions affected the distal femoropopliteal axis and the crural arteries. The mortality rates in our patients and in those of the TOPAS study indicate that the populations are comparable at least with respect to their general co-morbidity.

Eight patients (9%) in our series underwent major amputation, six below-knee, two above-knee, and one through-knee. In the TOPAS study the amputation-free survival rates in patients treated with urokinase were comparable to those achieved in the group with surgical treatment. However, there were 58 major amputations in the urokinase group (21%), 33 below-knee, and 25 above-knee. Thus, the percentage of amputees in the TOPAS study is significantly larger than in our series ($p<0.05$). The higher proportion of above-knee amputations ($p=0.01$) may be related to the more proximal disease. The 6 months amputation-free survival rate in our study was 82%, the 12 months amputation-free survival 78% (Fig. 4). In another prospective randomised study by Ouriel *et al.*,[6] the Rochester trial, the amputation-free survival rates at 1 year were 75% for the patients assigned to thrombolysis with urokinase, and 52% for those assigned to surgical treatment. Whilst the figures on local thrombolysis are similar in this report to our study with respect to the efficacy, there is a highly significant difference with regard to safety.

The mean dose of urokinase in the TOPAS study was 3.5 ± 1.8 millions IU, the mean duration of urokinase infusion 24.4 ± 14.2 h. In our study, the mean dose of urokinase was only $112\,500 \pm 55\,900$ IU. In the TOPAS study, there was a 12.5% major bleeding rate in the urokinase group, which increased further when patients received heparin. In four cases these haemorrhages were intracranial, and in one case fatal. The concomitant use of heparin had to be restricted during the course of the study. Transfusions of more than one unit of packed red cells were necessary in 92 patients (33.8%) in the urokinase group of the TOPAS study. This has been critically commented on in the accompanying editorial.[13] Also, the Rochester study[6] reported an 11% rate of serious bleeding complications in patients receiving urokinase, with one death due to haemorrhage. The STILE study[5] reported a 5.6% rate of serious haemorrhages in patients receiving thrombolytic agents, with low fibrinogen values identified as a risk factor. As stated earlier, there were no major haemorrhages in our study, accordingly no transfusions, and no surgical interventions for bleeding complications were necessary.

In the present study there were 28 legs (30%) that needed a secondary intervention; in 14 cases there was an endovascular and in 16 cases a surgical procedure. By contrast, in the TOPAS study urokinase group the percentage of secondary interventions was 55%, suggesting that routine primary catheter clot extraction, apart from avoiding major haemorrhage and shortening the procedure, provided better patency results, at least in the infrainguinal arteries.

Dotter[14] was the first to recognise the potential of selective clot lysis with low-dose streptokinase. Improvement of local lytic treatment was sought by infiltrating the thrombus directly using an end-hole catheter by Hess[1,2] rather than by perfusing the extremity with the thrombolytics. Schneider[10] used the microporous baloon catheter as applied in this study. Newer approaches are the pulsed or intraclot spray techniques.[15,16] All these techniques allow a reduction in the dose and time of thrombolysis. Schneider,[10] and later Starck *et al.*[11] demonstrated that percutaneous catheter clot aspiration and extraction were feasible, and a valuable addition to the armament of catheter therapy. By aspirating much, if not all, of the occluding clot the necessary dosage of lytic agent will be reduced significantly, and in fact render such medication unnecessary in a majority of cases. Thrombolysis serves rather to facilitate clot aspiration than to dissolve the whole volume of thrombus, and conversely percutaneous clot removal decreases the dose of urokinase. The end result is not only a reduction of the amount of thrombolytics but also of the time necessary to obtain patency, ranging from 35 to 160 min. The procedure is thus performed within the same time limits as a surgical intervention.The shorter duration of aspiration and adjunct interventions and the reduced exposure to thrombolytic agents are the factors we consider responsible for the lower rate of serious complications.

In conclusion, because of these advantages we recommend the combined catheter approach described above as first-line treatment for the segment of patients with acute or subacute occlusions in infrainguinal arteries. The intervention proposed in this series allows for clot aspiration, mild thrombolysis, and PTA as an "all-in-one" procedure, and is performed in local anaesthesia. Only a minority of cases will need modest amounts of lytic agents to obtain vascular patency. Hospitalisation time is reduced and patient comfort considerably enhanced.

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